Office of Education
Division of Intramural Research

Fellows Newsletter

October 2016

The Fellows Newsletter is published monthly by the Office of Education, Division of Intramural Research, National Heart, Lung, and Blood Institute and distributed to NHLBI DIR members to promote the interest of DIR Fellows.

NIH National Heart, Lung, and Blood Institute

In This Issue:

From the Director of the Office of Education

Fall has arrived, and with it we have a number of events planned. We've already had the first of our Career Development Seminars, and the Fellows Advisory Committee has a full schedule for the coming months, included in this Newsletter. We'll have our Halloween Bake-off on the 28th. This is a great way for the NHLBI DIR to display their creative talents in another format. Finally, we are in the planning stages for the next DIR Research Festival. Please send us your comments and suggestions as to how we might change/improve the festival for next year.

NHLBI DIR Halloween Bake-Off

Friday, October 28, 2016 | 3:00 - 4:00 PM
FAES Terrace, Building 10, NIH Main Campus




All NHLBI Fellows, Investigators, and Staff are invited.
Participate by bringing **baked goods OR $1**!
Baked goods must incorporate a Halloween theme, or at least orange and/or black.
All participants can vote for the winner, who will receive a cash prize!

Director's Column

Should I have a backup plan for my career?

By Dr. Herbert Geller

If you don't know where you are going, then what's next? There are two alternate quotes that begin with this phrase. One (paraphrased from *Alice in Wonderland*) ends with "any road'll take you there," while the other, from Yogi Berra (the great baseball player and manager whose malapropisms are legend) is, "If you don't know where you are going, you'll end up someplace else." When it comes to careers, it would seem like Yogi's quote is more apt, which is the reason that we continually ask Fellows to define their career goals.

Often, we get an answer, that "I hope for an academic career, but am preparing for alternates if that fails." This seems like a reasonable approach, given the vagaries of a scientific career. However, a recent paper entitled, "How backup plans can harm goal pursuit: the unexpected downside of being prepared for failure" (*Organizational Behavior and Human Decision Processes 135*:1-9, 2016) suggests that having alternate plans may actually impede success of the original plan.

The authors tested their hypothesis by asking study participants to participate in a game in which they could win a small monetary award. Some of the participants were told that there was a consolation prize, while others were not. The results were surprising: a higher percentage of those who needed to win the game to get the reward actually achieved success as compared to those who had the alternate option.

So how does this translate to career goals? One might say that if you are absolutely certain that only one career will make you happy, then you will focus all your efforts on achieving that goal, while if you have a backup plan for a different career, then you might put less effort into achieving your primary goal. The authors do point out that there is one situation where having a backup plan might not impede achieving a primary goal: if success depends upon factors which are not under the person's control. They allege that in this situation, having a backup is very realistic. On the other hand, when you have a strong desire for a certain outcome, then the effort should be directed at achieving that outcome; any effort at an alternate may be wasted. Overall, it would seem that for those who are highly motivated for one career (such as being a PI) having an alternate career plan early on could potentially be detrimental as it would channel energy away from the primary goal. The authors also point out that backup plans which are inherently undesirable may also provide positive motivation. Finally, these were laboratory experiments. Whether this actually obtains in real life situations, such as outcomes of postdoctoral training, needs further investigation.

Meet the New Fellows

Fei Mo is a new Postdoctoral Fellow in the Immunology Center under Dr. Warren Leonard. He earned his Ph.D. in Cell Biology from the University of Science and Technology of China. His lab is working with another on the engineering of interleukin 2 (IL-2), which shows promising effects for clinical treatment. He will further test the effects of these molecules in mice models. After his fellowship, he wishes to become an independent investigator in either academics or industry.

The Science Beat by Sarah Monti

Rhee, D. K., Lim, J. C., Hockman, S. C., **Ahmad, F.,** Woo, D. H., **Chung, Y. W.,** Liu, S., Hockman, A. L., & Manganiello, V. C. (2016). Effects of heterologous expression of human cyclic nucleotide Phosphodiesterase 3A (hPDE3A) on redox regulation in yeast. *Biochemical Journal*, BCJ20160572.

Cyclic AMP (cAMP), protein kinase A (PKA), and phosphodiesterase 3A (PDE3A) participate in a signaling loop in which cAMP activates PKA, which phosphorylates many proteins including PDE3A, and phosphorylated PDE3Ahydrolyzes cAMP. PKA regulation is implicated in control of metabolism, cell cycle, stress resistance, proliferation,and the proteasome pathway. Mutations in a PKA subunit can cause Carney complex in humans.

In their recent paper, Rhee *et al.* identified a novel PKA signaling pathway utilized in yeast during the oxidative stress response through heterologous expression of human cyclic nucleotide Phosphodiesterase 3A (hPDE3A). A yeast twohybrid library screening identified that hPDE3A interacts with an ubiquitin ligase. Expression of wild type (WT) hPDE3A and putative ubiquitinylation site mutants revealed that yeast expressing WT hPDE3A (OxiR1) were resistant

Continued on page 3

Meet the New Fellows

Faren Grant is a new Postdoctoral Fellow in the Cardiovascular and Pulmonary Branch under Dr. Tiffany Powell-Wiley. She earned her Ph.D. in Psychology with a concentration in Behavioral Medicine from the University of Maryland, Baltimore County, where she was also a Ph.D. researcher, research coordinator, and graduate research assistant. Faren has previously worked with the University of Michigan Department of Psychiatry and Emory University Department of Psychiatry and Behavioral Sciences in clinical research. Her project will be using her group's pre-existing data to explore the relation between stress and cardiometabolic biomarkers in a sample of urban-dwelling African American women. After her fellowship, she wishes to enter an academic professorship or a scientific officer position in a private company.

The Science Beat by Sarah Monti

to oxidative stress, whereas yeast expressing a K13R mutant (OxiS1) were sensitive to oxidative stress when compared to yeast expressing klempty vector (mock). This suggests that hPDE3A can contribute to regulation of redox homeostasis in a manner regulated by ubiquitinylation at K13.

Investigation of the mechanism by which hPDE3A regulates redox homeostasis revealed that the transcript level of the YAP1 mRNA for Yap1p, an important regulator of the oxidative stress response in yeast, varied in OxiR1, mock, and OxiS1 cells treated with hydrogen peroxide. OxiR1 cells showed the highest expression levels of YAP1, while mock cells showed increased YAP1 transcript levels, and the OxiS1 cells showed very little induction. Additionally, while the Yap1p proteins in OxiR1 cells were highly phosphorylated and these cells showed a corresponding increase in Yap1p-dependent antioxidant gene expression, the mock cells showed a lower level of phosphorylation and Yap1p-dependent gene expression, and the OxiS1 cells showed no apparent phosphorylation and no increase in expression of Yap1p-dependent genes. These results suggest that hPDE3A combats oxidative stress through activation of Yap1p and its dependent genes.

The first evidence that this redox regulation was not controlled by the traditional cAMP-PKA pathway was revealed by the similarity in cAMP levels across the different cell lines under oxidative stress conditions. Despite the similarity in cAMP levels in the varying cell lines, in the OxiR1 cells hPDE3A immunoprecipated with higher levels of PKA and showed higher levels of ubiquitinylation and phosphorylation compared to the K13R hPDE3A in the OxiS1 cells. The phosphorylation and ubiquitinylation levels of the hPDE3As correlated extremely well with cAMP-hydrolyzing activity.

Rhee *et al.* identified that in this system, instead of cAMP controlling PKA activity, Sch9p regulation of PKA determined the stress response. In OxiR1 and mock cells, oxidative stress inhibited Sch9p, an inhibitor of PKA, which allowed PKA activation and oxidative stress response. In OxiS1 cells, however, oxidative stress failed to inhibit Sch9p, allowing inhibition of PKA and compromising the cellular response to oxidative stress. This work provides evidence for a new pathway of PKA regulation and oxidative stress response. The means by which ubiquitinylation of PDE indirectly regulates PKA through Sch9p remains an exciting question to be pursued during further studies. ■

Recent Publications by NHLBI Fellows

Anandi, P., Tian, X., Chinian, F., **Cantilena, C. R.**, **Dunavin, N.**, Hensel, N., Draper, D., Koklanaris, E., Maxwell, S., Superata, J., Muranski, P., Battiwalla, M., Paczesny, S., Barrett, A. J., & Ito, S. (2016). Improved reproducibility and quality of GvHD biomarker assay: application of multiplex microfluidic channel system. *Bone Marrow Transplant*. 10.

Bhattacharya, P., Dey, R., Dagur, P. K., **Joshi, A. B.**, Ismail, N., Gannavaram, S., Debrabant, A., Akue, A. D., KuKuruga, M. A., Selvapandiyan, A., McCoy, J. P., Jr., & Nakhasi, H. L. (2016). Live Attenuated Leishmania donovani Centrin Knock Out Parasites Generate Non-inferior Protective Immune Response in Aged Mice against Visceral Leishmaniasis. *PLoS. Negl. Trop. Dis. 10*, e0004963.

Brady, O. A., **Diab, H. I.**, & Puertollano, R. (2016). Rags to riches: Amino acid sensing by the Rag GTPases in health and disease. *Small GTPases*. 1-10.

Chen, J. & Liu, J. (2016). Spindle Size Scaling Contributes to Robust Silencing of Mitotic Spindle Assembly Checkpoint. *Biophys. J.* 111, 1064-1077.

Jones, M. R., Brooks, B. R., & Wilson, A. K. (2016). Partition coefficients for the SAMPL5 challenge using transfer free energies. *J.*

Continued on page 4

Meet the New Fellows

Alessio Andreoni is a new Postdoctoral Fellow in the Biochemistry and Biophysics Center under Dr. Jay Knutson. He earned his Ph.D. in Biochemistry and Biophysics from Leiden University in the Netherlands, where he was a doctoral research associate. Alessio was previously a postdoctoral research associate at the Biodesign Institute at Arizona State University. His main focus is the further development of the STAQ technique for targetting intracellular structures, which is used to perform super-resolution microscopy using lower laser power than conventional techniques. This can eventually provide a system for cellular expression of fluorescent protein systems capable of STAQ, thus providing a way to do super-resolution with this method in living cells. His career goal is to pursue independent research in an environment with minimal teaching duties, so he can dedicate himself fully to scientific investigations. NIH, National Labs, as well as industry are all possible targets for this.

Recent Publications by NHLBI Fellows

Comput. Aided Mol. Des.

Khan, J. M., **Rogers, T.**, Schenke, W. H., Mazal, J. R., Faranesh, A. Z., Greenbaum, A. B., Babaliaros, V. C., Chen, M. Y., & Lederman, R. J. (2016). Intentional Laceration of the Anterior Mitral Valve Leaflet to Prevent Left Ventricular Outflow Tract Obstruction During Transcatheter Mitral Valve Replacement: Pre-Clinical Findings. *JACC. Cardiovasc. Interv. 9*, 1835-1843.

Konig, G., **Pickard, F. C.**, Huang, J., Simmonett, A. C., **Tofoleanu, F.**, **Lee, J.**, Dral, P. O., Prasad, S., Jones, M., Shao, Y., Thiel, W., & Brooks, B. R. (2016). Calculating distribution coefficients based on multi-scale free energy simulations: an evaluation of MM and QM/MM explicit solvent simulations of water-cyclohexane transfer in the SAMPL5 challenge. *J. Comput. Aided Mol. Des.*

Pickard, F. C., **Konig, G.**, **Tofoleanu, F.**, **Lee, J.**, Simmonett, A. C., Shao, Y., Ponder, J. W., & Brooks, B. R. (2016). Blind prediction of distribution in the SAMPL5 challenge with QM based protomer and pK a corrections. *J. Comput. Aided Mol. Des.*

Rhee, D. K., Lim, J. C., Hockman, S. C., **Ahmad, F.**, Woo, D. H., **Chung, Y. W.**, Liu, S., Hockman, A. L., & Manganiello, V. C. (2016). Effects of heterologous expression of human cyclic nucleotide Phosphodiesterase 3A (hPDE3A) on redox regulation in yeast. *Biochem. J.* BCJ20160572.

Rogers, T., Ratnayaka, K., Karmarkar, P., **Campbell-Washburn, A. E.**, Schenke, W. H., Mazal, J. R., Kocaturk, O., Faranesh, A. Z., & Lederman, R. J. (2016). Real-time magnetic resonance imaging guidance improves the diagnostic yield of endomyocardial biopsy. *JACC. Basic Transl. Sci. 1*, 376-383.

Q&A with an Investigator by Jodian Brown

Postdoctoral Fellow Jodian Brown interviews Dr. Courtney Fitzhugh.

Dr. Courtney Fitzhugh (M.D.) is currently a Lasker Clinical Research Scholar in the Sickle Cell Branch at NHLBI. She received her B.S. from the Univ. of California, Los Angeles (UCLA) and her M.D. from the Univ. of California, San Francisco (UCSF). She went on to complete her residency in internal medicine and pediatrics at Duke University Medical Center, followed by a combined adult hematology and pediatric hematology-oncology fellowship at NIH and Johns Hopkins Hospital. The central focus of her laboratory is on sickle cell disease (SCD) and the exploration of new therapeutic avenues involving hematopoietic stem cell (HSC) transplantation in the treatment of this disorder. HSC transplantation represents one of the few feasible cures for SCD.

What are the events that lead you to pursue SCD research and a career at NHLBI?

I became interested in sickle cell disease through two seminal events: a Christmas party for children with SCD that my mother organized at Children's Hospital Oakland, and then as an UCLA undergraduate preparing for medical school interviews, when I decided that this disease is one that I want to "find a cure" for.

My medical school training brought me to UCSF, where I entered the Medical Research Scholars Program and the laboratory of Dr. John Tisdale. Working with his group resulted in a protocol where they employed transplantation of HSC from the bone marrow of a complete matched sibling donor to SCD patient.

During my hematology fellowship, I decided to continue exploring novel approaches for HSC transplantation in SCD. The initial protocol requires a donor who is a complete tissue match, which limits the number of SCD patients that can be treated. As a result, I started developing a protocol that uses half-matched donors (e.g. any immediate genetic relatives such as parents and children) to donate stem cells, and potentially increases the number of patients that can be effectively treated.

As a clinical researcher, are there features of this position that impact your ability to strategize your research efforts?

As a clinician, two of my primary roles are

Continued on page 5

Q&A with an Investigator by Jodian Brown

to recruit patients and design protocols for study participants. I have the unique opportunity to directly evaluate the impact of each protocol on the patient population, and then to assess and determine the need to redesign existing or establish novel protocols.

However, I urge trainees who are interested in clinical research to learn basic laboratory methods that can help them better explore disease and treatment mechanisms associated with their protocol. A robust basic science training in concert to medical training is important when tackling such systemic disorders.

Did you experience any unexpected obstacle(s) along your career path to date?

Once I was accepted as a Clinical Tenure Track Investigator, which involved expanding my laboratory, I quickly realized the value and need for more basic science expertise to explore the types of research questions I am interested in. As a result, I hired a very talented Staff Scientist with the relevant expertise.

Did you always know that you wanted to pursue a career in clinical research? If no, what brought you to your decision of becoming a principal investigator?

Early on, I knew I wanted to be a clinical researcher. One defining moment was my appointment to Assistant Clinical Investigator in 2012. This opportunity simultaneously provided continued support through mentorship and independence via creation of my own laboratory. Through this experience, I gained the confidence and knowledge necessary to become a principal investigator.

What are your interests outside of research?

I am a member of Delta Sigma Theta Sorority, Inc. Currently, I chair the Physical and Mental Health Committee for the Montgomery County Alumnae Chapter, and I utilize this position to increase awareness of SCD. Also, I am actively engaged in my local church, where I currently serve as an usher.

What are some of the fun activities you engage in when away from the bench?

I love the outdoors, traveling (I recently went to the Dominican Republic), and cooking. I also enjoy going to the movies, plays, and concerts.

Can you offer some advice for trainees working towards independent scientific careers?

It is key to determine your passion—the scientific area and/or position that you are excited about. This will allow you to view work no longer as such, but as an opportunity to nurture your passion. Second, it is important to have good mentors, who should: i) have great communication skills, ii) be supportive, and iii) possess traits that you aspire to. Finally, prioritize a balanced life. ■

Meet the New Fellows

Molly Molloy is a new Postdoctoral Fellow in the Biochemistry and Biophysics Center under Dr. Jay Knutson. She earned her Ph.D. in Chemistry from Johns Hopkins University, where she was also a teaching assistant. Her project is to assess the feasibility of multiple dye molecules. By using lifetimes from FLIM and global analysis procedures, the hope is to be able to use and distinguish separate dyes all excited at the same wavelength in same acquisition. After her fellowship, she wishes to go into industry or government research.

Selami Demirci is a new Postdoctoral Fellow in the Sickle Cell Branch under Dr. John Tisdale. He earned his Ph.D. in Genetics and Bioengineering from Yeditepe University in Turkey, where he was also a research assistant and postdoctoral researcher. His project involves establishment in vitro culture model to develop erythroid differentiation for rhesus cells. After his fellowship, he wishes to return to Turkey to establish his own laboratory, and become a mentor.

Sayuri Higashi is a new Predoctoral Fellow in the Cell Biology and Physiology Center under Dr. Herbert Geller. She is earning her Master's degree in Biochemistry at Gifu University, Japan, where she was also a teaching assistant. Her project is developing RNA medicine that is delivered to target tissue by conjugating antibody mimic, and she would like to go into academics after her fellowship.

Jeong-A Lim is a new Postdoctoral Fellow in the Cell Biology and Physiology Center under Dr. Rosa Puertollano Moro. She earned her Ph.D. in Biology from Ajou University. She was previously a postdoctoral research fellow at the National Cancer Center in South Korea, the Telethon Institute of Genetics and Medicine in Italy, and at NIAMS. Her project focuses on transcription factor EB and E3 as therapeutic targets for the treatment of lysosomal storage diseases. After her fellowship, she would like to go into academics, and keep studying lysosomal storage diseases.

Lenfant Biomedical Fellowship Awardees

The Lenfant Biomedical Fellowship is a competitive award granted to outstanding NHLBI DIR postdoctoral fellows who are committed to pursuing a career in research. Recipients of the Lenfant fellowship will receive an increase in stipend support (up to 10%) depending on their employment mechanism.

The next cycle's deadline is October 15, 2016. For instructions and more funding opportunities, please visit our Intranet at: https://intranet.nhlbi.nih.gov/general/postdoctoral-fellowships-open-to-nhlbi-intramural-fellows.

Congratulations to the awardees from the most recent cycle:

Heather Teague under Dr. Nehal Mehta with "Human Translational Studies of Neutrophil Subsets: A Novel Link to Atherogenesis in Psoriasis?"

Jessica Flynn under Dr. Jennifer Lee with "Developing Raman Microscopy for Studying alpha-Synuclein Aggregation in Cellular Environments"

Madeleine Davison under Dr. Nico Tjandra with "Structure based drug design of a novel HIV 1 inhibitor"

Career Development Series

The NHLBI DIR Fellows Advisory Committee is hosting a monthly Career Development Series in Fall 2016, featuring science career panelists, some of whom were previously NIH fellows. These informal panel Q&A sessions are aimed at postdoctoral fellows, but anyone is welcome!

Thank you everyone who attended the September session on careers in sales. Please stay tuned for more details and RSVP emails, and see below for the schedule:

- Thursday, October 27, BLDG 50 RM 2328, 3:30-4:30PM: Patent Law
- Thursday, November 10, BLDG 50 RM 2328, 4:00-5:00PM: Regulatory Affairs
- Wednesday, December 7, BLDG 50 RM 2328, 4:00-5:00PM: Consulting

From the NIH Fellows Committee

- Come to the International Opportunties Expo on Thursday, October 20, 2016 on the FAES Terrace from 1:30 to 4:00PM! Please visit the website for more information: https://www.training.nih.gov/international_expo_presentations
- The Career Development Committee will host their next panel on "Careers in Biotech" on Tuesday, October 18 at 3:00PM in Building 50, Room 1227.
- FAES needs your help in completing an NIH-wide Fellows Health and Dental Insurance Survey. Please follow the link to participate: https://www.surveymonkey.com/r/M785KK2.
- FAES is offering BioTech Training courses and workshops. Please visit https://faes.org/content/biotech-workshops-0 for more information.

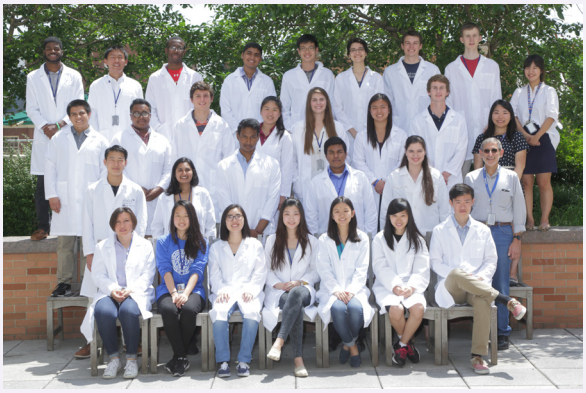
2016-2017 NHLBI DIR Tenure Track Seminar Series

This series is sponsored by the NHLBI Office of Education and Tenure Track Investigators, and draws a diverse audience from all areas of science represented in the NHLBI Intramural Research Program.

- Nov. 29, 2016; 11 AM, BLDG 50 RM 1227/1233: David Drubin, Ph.D., University of California, San Francisco
- Jan. 24, 2017; 11 AM, BLDG 50 RM 1227/1233: Andrew Dillin, Ph.D., University of California, Berkeley
- Jan. 31, 2017; 11 AM, BLDG 50 RM 1227/1233: Christopher Burge, Ph.D., Massachusetts Institute of Technology
- Feb. 14, 2017; 11 AM, BLDG 50 RM 1227/1233: Raul Andino, Ph.D., University of California, San Francisco
- Feb. 28, 2017; 11 AM, BLDG 50 RM 1227/1233: David Harrison, M.D., Vanderbilt University
- Mar. 7, 2017; 11 AM, BLDG 50 RM 1227/1233: Anne Hart, Ph.D., Brown University
- Mar. 14, 2017, 11 AM, BLDG 50 RM 1227/1233: Dennis Discher, Ph.D., University of Pennsylvania
- Mar. 28, 2017, 11 AM, BLDG 50 RM 1227/1233: Alan Saltiel, Ph.D., University of California, San Diego
- May 2, 2017, 11 AM, BLDG 50 RM 1227/1233: Ruth Lehmann, Ph.D., New York University
- May 16, 2017, 11 AM, BLDG 50 RM 1227/1233: Jagat Narula, M.D., Ph.D., M.A.C.C., Icahn School of Medicine at Mount Sinai
- May 30, 2017, 11 AM, BLDG 50 RM 1227/1233: David Agard, Ph.D., University of California, San Francisco
- Jun. 13, 2017, Details TBA: Courtney DiNardo, M.D., M.S.C.E., University of Texas

Summer Internship Program

Supervising a summer intern is a great way to get mentoring experience. The website for summer internship applications will open in mid-November. Please look forward to emails from the Office of Education for more policies and directions on accepting students. Thank you for making the 2015 SIP a success, and we look forward to the summer of 2016!



NHLBI Fellows Advisory Committee

FAC is always looking for new members! If you would like to represent your lab on Fellows issues, and have a say in future NHLBI events and activities, including the Annual NHLBI DIR Research Festival, please join the FAC by emailing us at: DIREDUCATION@NHLBI.NIH.GOV. Meetings are every second Monday of each month from 4 to 5PM in Building 50, Room 4229.

If you have any comments or concerns regarding your fellowship, please also feel free to contact our office.

NHLBI Skype Room

The NHLBI Skype Room (Building 10, Room 4-1581) has recently opened for use! The room is a small, enclosed office with a Mac desktop available for online meetings. The room is located in the Scientific Director's office - from the 1st floor of the North lobby of the Hatfield Center, take the northwest elevators to the 4th floor. Exit straight out of the elevators, and the OSD is just to the right (same side as the elevators, look for the women's restroom). To schedule the room, please contact Hillary Flowers at 301-496-2116 or hillary.flowers@nih.gov at least **1 business day in advance** of your meeting.